FIGURE 1A

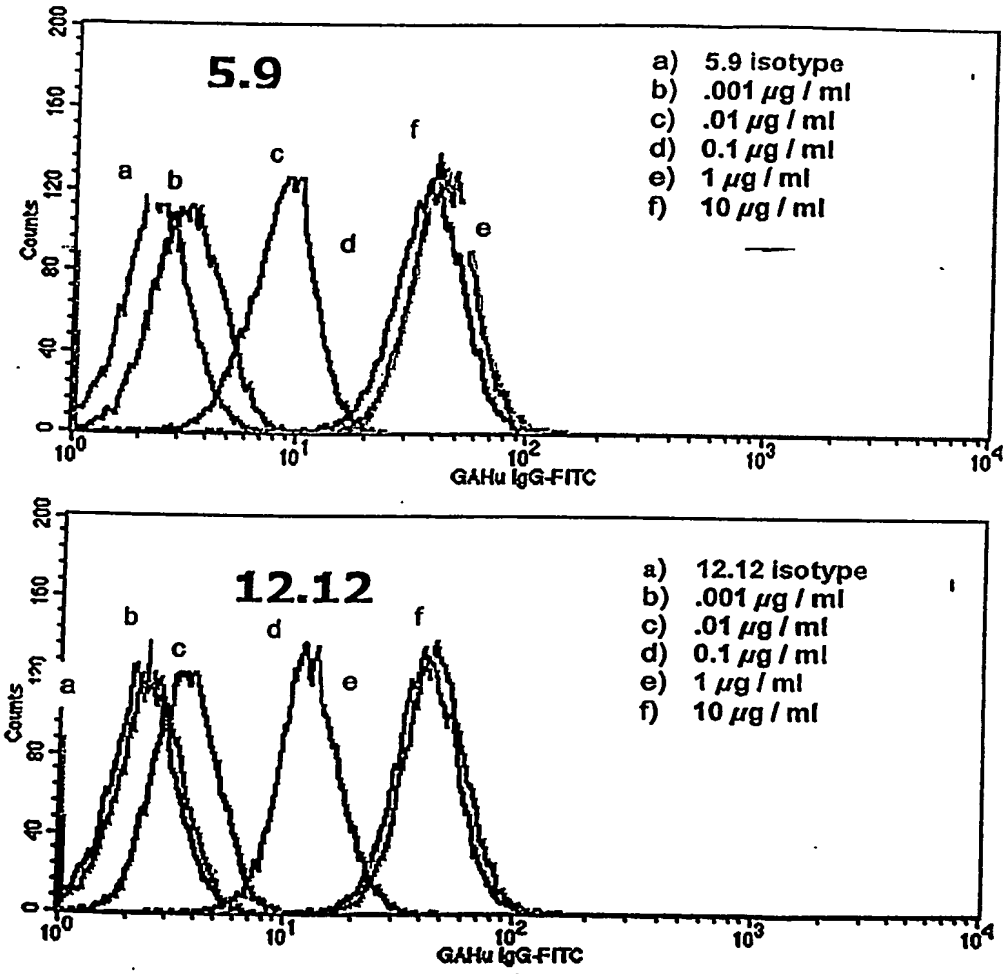

FIGURE 1B

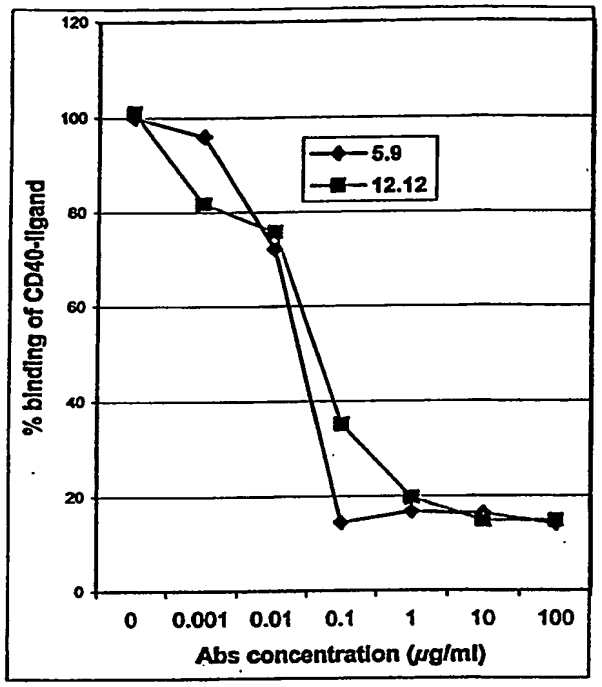
120
100
80
60
40
20
0
% binding of CD40-ligand
5.9
12.12
0
0.001
0.01
0.1
1
10
100
Abs concentration (μg/ml)

FIGURE 2A

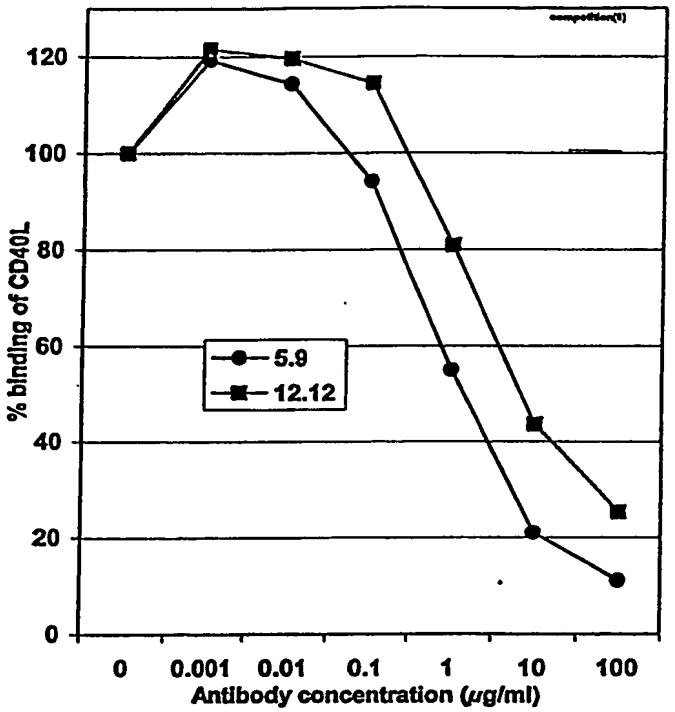
120
100
80
60
40
20
0
% binding of CD40L
5.9
12.12
0
0.001
0.01
0.1
1
10
100
Antibody concentration (μg/ml)

FIGURE 2B

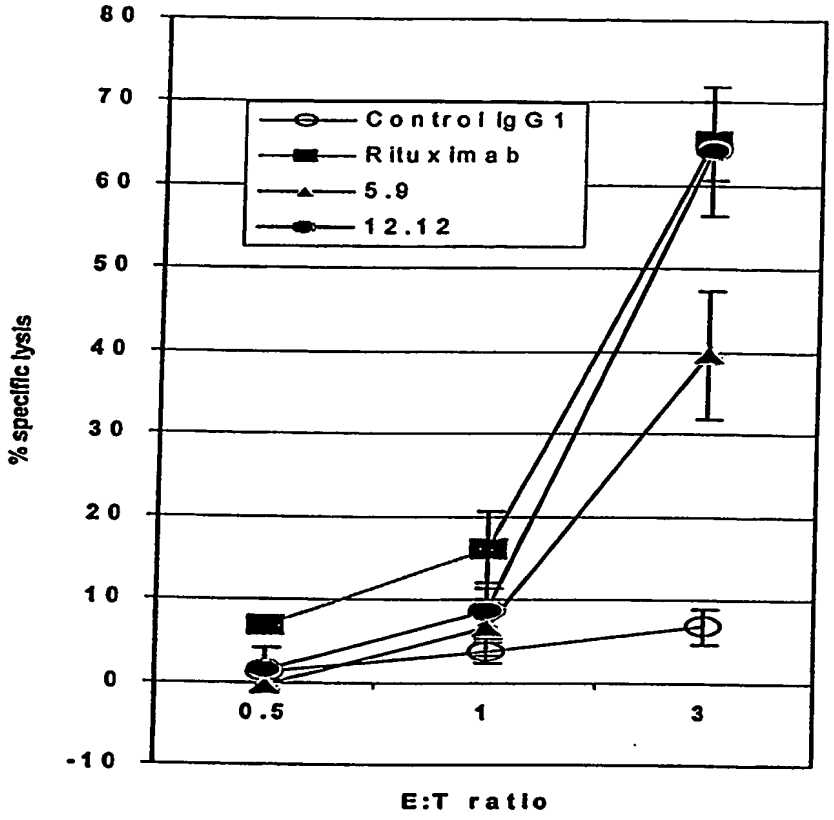
80
70
60
50
40
30
20
10
0
-10
% specific lysis
Control IgG1
Rituximab
5.9
12.12
0.5
1
3
E:T ratio

FIGURE 3A

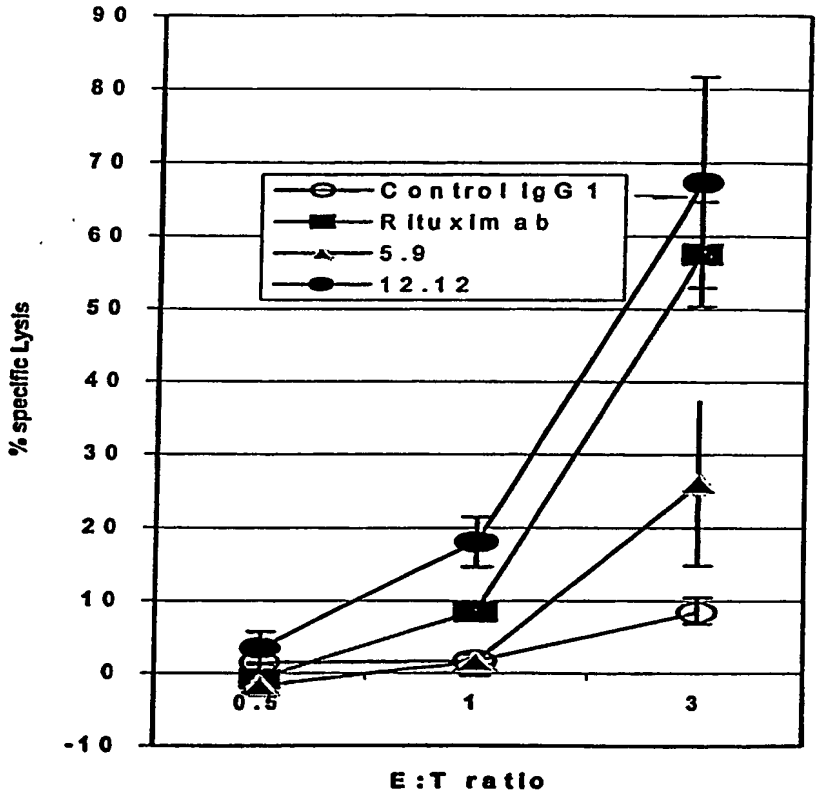
90
80
70
60
50
40
30
20
10
0
-10
% specific Lysis
Control IgG 1
Rituximab
5.9
12.12
0.5
1
3
E:T ratio

FIGURE 3B

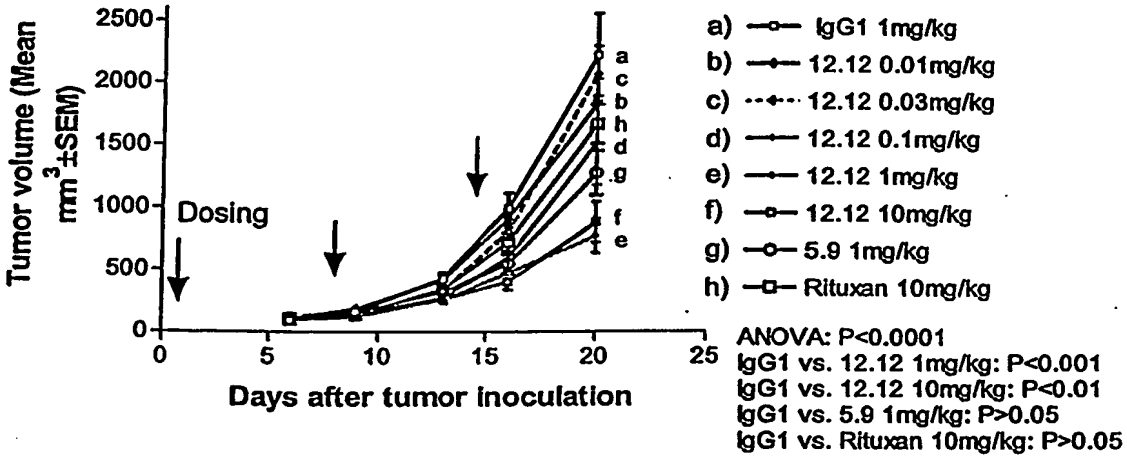
Tumor volume (Mean mm3±SEM)
2500
2000
1500
1000
500
0
Dosing
0
5
10
15
20
25
Days after tumor inoculation
a
c
b
h
d
g
f
e
a) IgG1 1mg/kg
b) 12.12 0.01mg/kg
c) 12.12 0.03mg/kg
d) 12.12 0.1mg/kg
e) 12.12 1mg/kg
f) 12.12 10mg/kg
g) 5.9 1mg/kg
h) Rituxan 10mg/kg
ANOVA: P<0.0001
IgG1 vs. 12.12 1mg/kg: P<0.001
IgG1 vs. 12.12 10mg/kg: P<0.01
IgG1 vs. 5.9 1mg/kg: P>0.05
IgG1 vs. Rituxan 10mg/kg: P>0.05

FIGURE 4

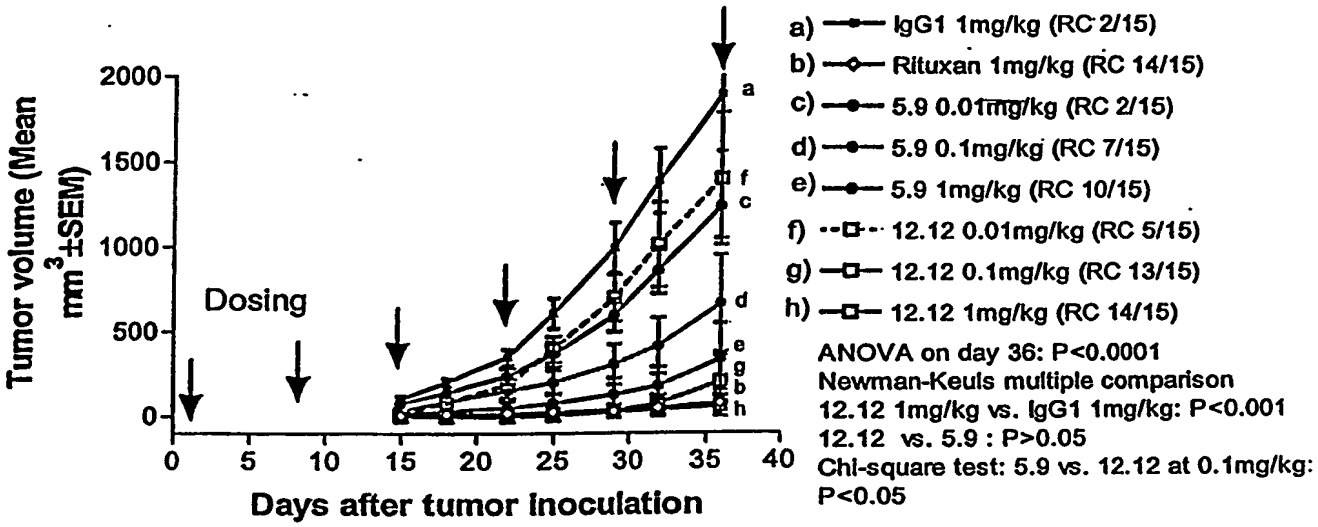
Tumor volume (Mean mm3 ±SEM)
2000
1500
1000
500
0
Dosing
0
5
10
15
20
25
30
35
40
Days after tumor inoculation
a
f
c
d
e
g
b
h
a) IgG1 1mg/kg (RC 2/15)
b) Rituxan 1mg/kg (RC 14/15)
c) 5.9 0.01mg/kg (RC 2/15)
d) 5.9 0.1mg/kg (RC 7/15)
e) 5.9 1mg/kg (RC 10/15)
f) 12.12 0.01mg/kg (RC 5/15)
g) 12.12 0.1mg/kg (RC 13/15)
h) 12.12 1mg/kg (RC 14/15)
ANOVA on day 36: P<0.0001
Newman-Keuls multiple comparison
12.12 1mg/kg vs. IgG1 1mg/kg: P<0.001
12.12 vs. 5.9 : P>0.05
Chi-square test: 5.9 vs. 12.12 at 0.1mg/kg:
P<0.05

FIGURE 5

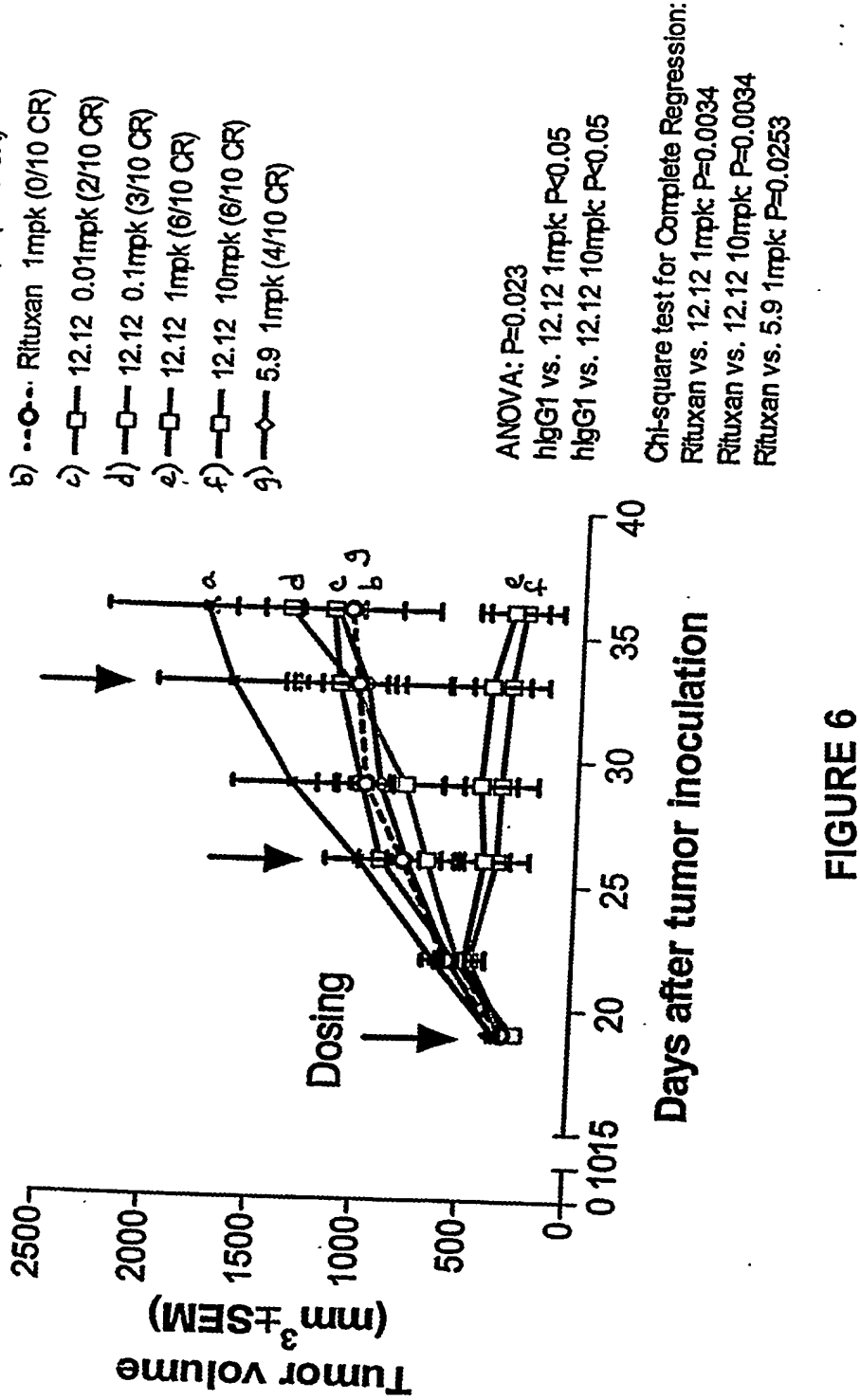
a) hIgG1 1mpk (2/10 CR)
b) Rituxan 1mpk (0/10 CR)
c) 12.12 0.01mpk (2/10 CR)
d) 12.12 0.1mpk (3/10 CR)
e) 12.12 1mpk (6/10 CR)
f) 12.12 10mpk (6/10 CR)
g) 5.9 1mpk (4/10 CR)
ANOVA: P=0.023
hIgG1 vs. 12.12 1mpk: P<0.05
hIgG1 vs. 12.12 10mpk: P<0.05
Chi-square test for Complete Regression:
Rituxan vs. 12.12 1mpk: P=0.0034
Rituxan vs. 12.12 10mpk: P=0.0034
Rituxan vs. 5.9 1mpk: P=0.0253
Tumor volume (mm³±SEM)
2500
2000
1500
1000
500
0
0 10 15 20 25 30 35 40
Days after tumor inoculation
Dosing

FIGURE 6

Number of CD20 and CD40 Molecules on Namalwa and Daudii Cells

Methods:

1. Harvest and wash cells once with PBS w/o Ca++/Mg++ plus 0.5%BSA and 0.1% Sodium Azide.
2. Block 1e5 cells with 10% huSerum in PBS w/o Ca++/Mg++ plus 0.1% Sodium Azide on ice for 30 minutes.
3. Stain cells with FITC conjugated antibodies (12.12-FITC or Rituximab-FITC) on ice for 40minutes. Cells were also stained with huIgG1-FITC for non-specific binding control. Antibody concentrations were 0.01, 0.1, 1, 10 and 100ug per ml.
4. Determine Mean Channel Fluorescence (Geometric Mean) by flow cytometer using log amplifier. PI was added to exclude dead cells.
5. Determine Mean Channel Fluorescence (Geometric Means) of Quantum™24FITC (3,000 to 5,000 MESF*), QuantumTM[25]FITC (50,000 to 2,000,000 MESF) and Quantum™26FITC (10,000 to 500,000 MESF) at the same instrument settings as for samples analysis.
MESF: Molecules of Equivalent Soluble Fluorochrome
6. Construct calibration curve by plotting MESF (y-axis) vs. the Geometric Means (x-axis).
7. The number of molecules per cell was determined using the following equation: y=ax^b where y is equal to MESF and x is equal to Mean Channel Fluorescence of the sample. Mean Channel Fluorescence used for each sample was the Geo Mean at saturation concentration (12.12FTIC) or the highest concentration (rituximabFITC).
8. Dividing MESF of sample by the numbers of FITC molecules conjugated to each antibody (F:P ratio) to determine the antibody binding capacity (ABC). ABC of huIgGFITC of respected sample was corrected to obtain the final antibody binding capacatiy.

	Daudii		Namalwa	
Exp.	CD40	CD20	CD40	CD20
E090403	14403.0	93676.5	3296.4	6200.1
E091003	13214.9	108438.5	3081.5	4788.2
E091103	13702.6	100509.1	3165.7	3988.3
E091203	13278.9	128158.3	3164.9	4618.0
Average	**13,649.9**	**107,695.6**	**3,177.1**	**4,898.7**
Stdev	546.7	14915.9	88.8	933.4

FIGURE 7

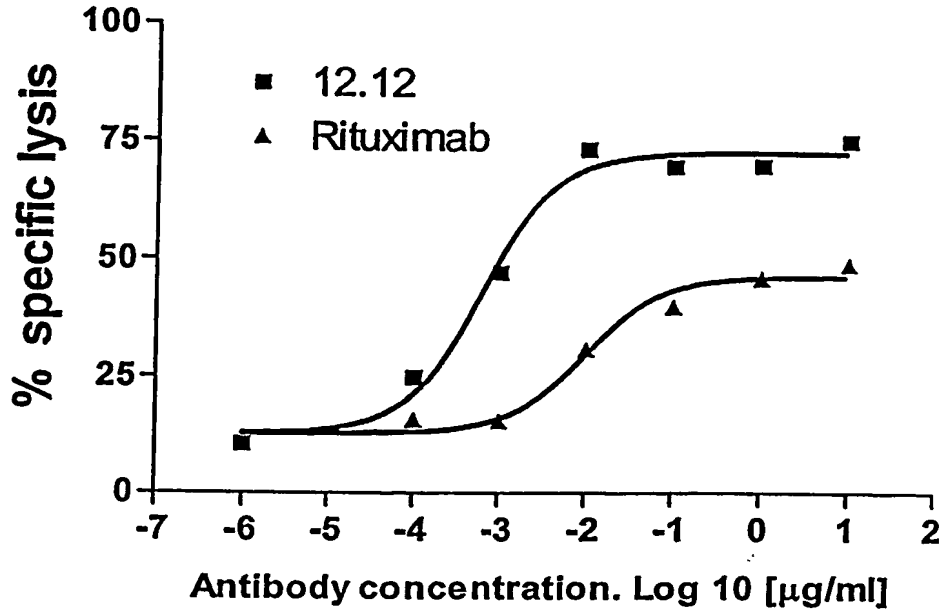
100
75
50
25
0
% specific lysis
12.12
Rituximab
-7
-6
-5
-4
-3
-2
-1
0
1
2
Antibody concentration. Log 10 [µg/ml]

FIGURE 8

FIGURE 9A

CHIR 12.12 light chain:

leader:

MALPAQLLGLLMLWVSGSSG

variable:

DIVMTQSPLSLTVTPGEPASISCRSSQSLLYSNGYNYLDWYLQKPGQSPQVLISLGSNRASG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQARQTPFTFGPGTKVDIR

constant:

RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK
DSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 9B

CHIR-12.12 heavy chain:

leader:

MEFGLSWVFLVAILRGVQC

variable:

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYEESNRYHAD
SVKGRFTISRDNSKITLYLQMNSLRTEDTAVYYCARDGGIAAPGPDYWGQGTLVTVSS

constant:

ASTKGPSVFPLAPASKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVF
LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV
SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL
TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

alternative constant region:

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVF
LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV
SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL
TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

FIGURE 10A

DNA sequence of light chain of CHIR-12.12:

5'atggcgctccctgctcagctcctggggctgctaatgctctgggtctctggatccagtggggatattgtgatgactcagtctccactctc
cctgaccgtcacccctggagagccggcctccatctcctgcaggtccagtcagagcctcctgtatagtaatggatacaactatttggattg
gtacctgcagaagccagggcagtctccacaggtcctgatctctttgggttctaatcgggcctccggggtccctgacaggttcagtggca
gtggatcaggcacagattttacactgaaaatcagcagagtggaggctgaggatgttggggtttattactgcatgcaagctcgacaaact
ccattcactttcggccctgggaccaaagtggatatcagacgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagt
tgaaatctggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacagtggaaggtggataacgccctcc
aatcgggtaactcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcctcagcagcaccctgacgctgagcaa
agcagactacgagaaacacaaagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagcttcaacaggg
gagagtgttag3'

FIGURE 10B

DNA sequence of heavy chain of CHIR-12.12 (including introns):

5'atggagtttgggctgagctgggttttccttgttgctattttaagaggtgtccagtgtcaggtgcagttggtggagtctgggggaggcgt
ggtccagcctgggaggtccctgagactctcctgtgcagcctctggattcaccttcagtagctatggcatgcactgggtccgccaggctc
caggcaaggggctggagtgggtggcagttatatcatatgaggaaagtaatagataccatgcagactccgtgaagggccgattcacca
tctccagagacaattccaagatcacgctgtatctgcaaatgaacagcctcagaactgaggacacggctgtgtattactgtgcgagagat
gggggtatagcagcacctgggcctgactactggggccagggaaccctggtcaccgtctcctcagcaagtaccaagggcccatccgt
cttccccctggcgcccgctagcaagagcacctctgggggcacagcggccctgggctgcctggtcaaggactacttccccgaaccgg
tgacggtgtcgtggaactcaggcgccctgaccagcggcgtgcacaccttcccggctgtcctacagtcctcaggactctactccctcag
cagcgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgcaacgtgaatcacaagcccagcaacaccaaggtgg
acaagagagttggtgagaggccagcacagggagggagggtgtctgctggaagccaggctcagcgctcctgcctggacgcatcccg
gctatgcagtcccagtccagggcagcaaggcaggccccgtctgcctcttcacccggaggcctctgcccgccccactcatgctcagg
gagagggtcttctggctttttccccaggctctgggcaggcacaggctaggtgcccctaacccaggccctgcacacaaaggggcaggt
gctgggctcagacctgccaagagccatatccgggaggaccctgcccctgacctaagcccaccccaaaggccaaactctccactccc
tcagctcggacaccttctctcctcccagattccagtaactcccaatcttctctctgcagagcccaaatcttgtgacaaaactcacacatgc
ccaccgtgcccaggtaagccagcccaggcctcgccctccagctcaaggcgggacaggtgccctagagtagcctgcatccagggac
aggccccagccgggtgctgacacgtccacctccatctcttcctcagcacctgaactcctgggggggaccgtcagtcttcctcttcccccc
aaaacccaaggacaccctcatgatctcccggacccctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtca
agttcaactggtacgtggacggcgtggaggtgcataatgccaagacaaagccgcgggaggagcagtacaacagcacgtaccgtgt
ggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaaggagtacaagtgcaaggtctccaacaaagccctcccagccc
ccatcgagaaaaccatctccaaagccaaaggtgggacccgtggggtgcgagggccacatggacagaggccggctcggcccaccc
tctgccctgagagtgaccgctgtaccaacctctgtccctacagggcagccccgagaaccacaggtgtacaccctgcccccatcccgg
gaggagatgaccaagaaccaggtcagcctgacctgcctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa
tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccgacggctccttcttcctctatagcaagctcaccgtggac
aagagcaggtggcagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaaccactacacgcagaagagcctctcc
ctgtctccgggtaaatga3'

FIGURE 11A

CHIR-5.9 light chain:

leader:

MALLAQLLGLLMLWVPGSSG

variable:

AIVMTQPPLSSPVTLGQPASISCRSSQSLVHSDGNTYLNWLQQRPGQPPRLLIYKFFRRLSG
VPDRFSGSGAGTDFTLKISRVEAEDVGVYYCMQVTQFPHTFGQGTRLEIK

constant:

RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK
DSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIGURE 11B

CHIR-5.9 heavy chain:

leader:

MGSTAILALLLAVLQGVCA

variable:

EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGDSDTRYSP
SFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARGTAAGRDYYYYYGMDVWGQGTTVTVS
S

constant:

ASTKGPSVFPLAPASKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVF
LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV
SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL
TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

alternative constant region:

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVF
LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV
SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL
TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

FIGURE 12A

Coding sequence for short isoform of human CD40:

```
  1 atggttcgtc tgcctctgca gtgcgtcctc tggggctgct tgctgaccgc tgtccatcca
 61 gaaccaccca ctgcatgcag agaaaaacag tacctaataa acagtcagtg ctgttctttg
121 tgccagccag gacagaaact ggtgagtgac tgcacagagt tcactgaaac ggaatgcctt
181 ccttgcggtg aaagcgaatt cctagacacc tggaacagag agacacactg ccaccagcac
241 aaatactgcg accccaacct agggcttcgg gtccagcaga agggcacctc agaaacagac
301 accatctgca cctgtgaaga aggctggcac tgtacgagtg aggcctgtga gagctgtgtc
361 ctgcaccgct catgctcgcc cggctttggg gtcaagcaga ttgctacagg ggtttctgat
421 accatctgcg agccctgccc agtcggcttc ttctccaatg tgtcatctgc tttcgaaaaa
481 tgtcaccctt ggacaaggtc cccaggatcg gctgagagcc ctggtggtga tccccatcat
541 cttcgggatc ctgtttgcca tcctcttggt gctggtcttt atcaaaaagg tggccaagaa
601 gccaaccaat aa
```

FIGURE 12B

Encoded short isoform of human CD40:

```
  1 mvrlplqcvl wgclltavhp epptacrekq ylinsqccsl cqpgqklvsd cteftetecl
 61 pcgesefldt wnrethchqh kycdpnlglr vqqkgtsetd tictceegwh ctseacescv
121 lhrscspgfg vkqiatgvsd ticepcpvgf fsnvssafek chpwtrspgs aespggdphh
181 lrdpvchplg aglyqkggqe anq
```

FIGURE 12C

Coding sequence for long isoform of human CD40:

```
   1 atggttcgtc tgcctctgca gtgcgtcctc tggggctgct tgctgaccgc tgtccatcca
  61 gaaccaccca ctgcatgcag agaaaaacag tacctaataa acagtcagtg ctgttctttg
 121 tgccagccag gacagaaact ggtgagtgac tgcacagagt tcactgaaac ggaatgcctt
 181 ccttgcggtg aaagcgaatt cctagacacc tggaacagag agacacactg ccaccagcac
 241 aaatactgcg accccaacct agggcttcgg gtccagcaga agggcacctc agaaacagac
 301 accatctgca cctgtgaaga aggctggcac tgtacgagtg aggcctgtga gagctgtgtc
 361 ctgcaccgct catgctcgcc cggctttggg gtcaagcaga ttgctacagg ggtttctgat
 421 accatctgcg agccctgccc agtcggcttc ttctccaatg tgtcatctgc tttcgaaaaa
 481 tgtcaccctt ggacaagctg tgagaccaaa gacctggttg tgcaacaggc aggcacaaac
 541 aagactgatg ttgtctgtgg tccccaggat cggctgagag ccctggtggt gatccccatc
 601 atcttcggga tcctgtttgc catcctcttg gtgctggtct ttatcaaaaa ggtggccaag
 661 aagccaacca ataaggcccc ccaccccaag caggaacccc aggagatcaa ttttcccgac
 721 gatcttcctg gctccaacac tgctgctcca gtgcaggaga ctttacatgg atgccaaccg
 781 gtcacccagg aggatggcaa agagagtcgc atctcagtgc aggagagaca gtga
```

FIGURE 12D

Encoded long isoform of human CD40:

```
   1 mvrlplqcvl wgclltavhp epptacrekq ylinsqccsl cqpgqklvsd cteftetecl
  61 pcgeseftdt wnrethchqh kycdpnlglr vqqkgtsetd tictceegwh ctseacescv
 121 lhrscspgfg vkqiatgvsd ticepcpvgf fsnvssafek chpwtscetk dlvvqqagtn
 181 ktdvvcgpqd rlralvvipi ifgilfaill vlvfikkvak kptnkaphpk qepqeinfpd
 241 dlpgsntaap vqetlhgcqp vtqedgkesr isvqerq
```

FIGURE 13